

# Diffusion Weighted MRI Patterns Caused by Acute Border Zone Infarction<sup>1</sup>

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**Purpose:** We investigated the causes and mechanisms driving acute border zone infarctions using diffusion-weighted imaging (DWI).

**Materials and Methods:** We analyzed DWI in 104 patients (male: 72 years, female: 32 years, age range: 44 to 84 years) with acute border zone infarction. The DWI patterns were classified as follows: pattern A- An acute border zone infarction combined with multiple small disseminated cortical infarctions, pattern B- An acute border zone infarction only.

**Results:** The most common cause of acute border zone infarctions was extracranial internal carotid artery (ICA) stenosis (45 cases, 43%). Other causes included middle cerebral artery stenosis (22 cases, 21%), intracranial ICA stenosis (14 cases, 13%), unknown, (12 cases 12%), iatrogenic (6 cases, 6%) and cardiogenic (5 cases, 5%), respectively. The most common pattern for DWI was pattern A (83 cases, 80%). We performed a transcranial Doppler in 7 of 75 cases (11%), and found at least 1 embolic pulse.

**Conclusion:** The most common pattern of DWI for acute border zone infarctions was pattern A. We propose that the mechanisms driving acute border zone infarctions are emboli coupled with hypoperfusion.

**Index words :** Brain infarction

Diffusion magnetic resonance imaging

Cerebral infarction

Several studies have addressed the possible mechanisms contributing to acute border zone infarctions. These include hemodynamic factors, embolic factors or both (1 - 6), and were determined by a transcranial

Doppler (TCD) study and autopsies (7, 8).

Before the era of magnetic resonance imaging (MRI), a computed tomography (CT) was the only method for diagnosing infarctions; however, due to limited resolution, subtle lesions caused by disseminated cortical infarctions could not be determined. The advent of diffusion-weighted imaging (DWI) led to the ability of identifying subtle lesions accompanied with acute border zone infarctions; namely disseminated cortical infarctions consisting of scattered small cortical high signal intensities.

Occlusion or stenosis of the intracranial or extracra-

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nial cerebral arteries is recognized as the cause leading to acute border zone infarctions; however, the mechanisms driving them, such as the postulated decreased perfusion or emboli are still unclear.

In this study, we investigated the causes of acute border zone infarctions as well as the lesion patterns generated using DWI, in order to confirm the mechanisms driving acute border zone infarctions.

## Materials and Methods

### Patients

We analyzed 104 patients (male: 72 patients, female: 32 patients) ranging in age from 44 to 84 years of age (mean age: 69 years) and who visited the — University Hospital between May of 2005 and December of 2006. The patients had suspected acute border zone infarctions. The inclusion criteria were as follows: 1) the patient had an acute border zone infarction which was visible on DWI, 2) the patient's lesions were located in the supratentorial area, 3) the patient underwent a magnetic resonance angiography (MRA) or conventional angiography, 4) the patient had to evaluate a cardiac issue using a trans-esophageal echocardiography or 24-hour electrocardiography (ECG) monitoring. We excluded patients with tandem lesions in the internal carotid artery (ICA) and middle cerebral artery (MCA). A total of 104 patients satisfied the inclusion criteria.

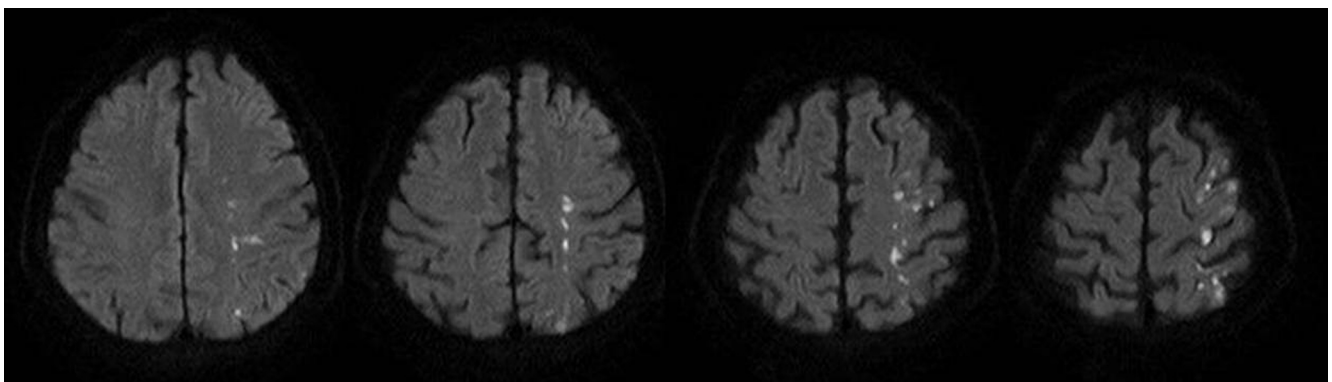
### MRI studies

All patients underwent DWI using a 1.5-T MR imaging unit (Intera, Philips Medical Systems, Best, Netherlands) with echo-planar capabilities. The acute border zone infarction is described as a high signal intensity image which is visible on DW, and located in the

white matter along and slightly above the lateral ventricle, between the deep and the superficial arterial systems of the MCA. Alternatively, the cortical border zone infarction is described as a high signal intensity image which is visible on DW, and was located between the cortical region of the anterior cerebral artery (ACA), MCA, and the posterior cerebral artery (PCA). A disseminated cortical infarction is defined as small hyperintense spots in the cortex, and is attributed to concomitant emboli. A combined infarction pattern with an acute border zone infarction is described as follows; 1) Pattern A: An acute border zone infarction combined with multiple small disseminated cortical infarctions (Fig. 1A). 2) Pattern B: an acute border zone infarction only, (Fig. 2A, B). Pattern A represents fragmented emboli or multiple micro-emboli in the distal territory of MCA, whereas Pattern B represents an acute border zone infarction which was not combined with any other types of infarctions. A three-dimensional time-of-flight (TR: 17 msec, TE: 6.9 msec, flip angle: 20 °, matrix: 240 × 512, thickness: 1.3 mm, NEX: 1), and contrast enhanced MRA (TR: 4.3 msec, TE: 1.61 msec, flip angle: 40 °, matrix: 448 × 512, thickness: 2.2 mm, NEX: 1) was performed to evaluate the degree of stenosis, proximal ICA, and MCA. Fifteen milliliters of contrast agent (Gadovist 1.0, Schering AG, Berlin, Germany) was injected at a rate of 3 ml/sec through the antecubital vein.

### Measurement of arterial stenosis

We measured the degree of the ICA stenosis on a MRA or conventional angiography. We classified the degree of stenosis into 4 categories: mild (less than 50%), moderate (50% to 70%), severe (70% to 90%) and near-complete or complete occlusion (more than 90%). Also, we graded the MCA lesions into 2 categories: stenosis



**Fig. 1.** Pattern A: An acute internal border zone infarction combined with multiple disseminated cortical infarctions is captured by diffusion-weighted imaging. The etiology is unknown.

and occlusion.

### Transcranial Doppler Ultrasound Examination

We performed a TCD to detect the embolic signal. The distal segment of the MCA was examined through a temporal window for 30 min, in 75 of 104 patients. The definition of an embolic signal was as follows: a typically visible and audible (click, chirp, and whistle), short duration, high-intensity signal within a Doppler flow spectrum with an occurrence at random in the cardiac cycle, and an increase in intensity by 5 dB or more above the background signal. The presence of embolic signals was determined by a neurologist with no prior knowledge of the patient's data.

## Results

### Causes of acute border zone infarctions

The causes of acute border zone infarctions were classified into four categories: 1) intra- or extra-cranial arterial, 2) cardiogenic, 3) iatrogenic (post-conventional angiography), 4) unknown. The intra- or extra-cranial arterial causes were further classified based on the location of lesions: 1) proximal ICA, 2) distal ICA and, 3) MCA. The most common cause for border zone infarctions was a proximal ICA stenosis or an occlusion (45 cases, 43%), followed by a MCA stenosis or an occlusion (22 cases, 21%), a distal ICA stenosis (14 cases, 13%), unknown (12 cases, 12%), iatrogenic (6 cases, 6%), and cardiogenic in 5 cases (5%) (Fig. 3).

### DWI patterns of acute border zone infarction according to causes

DWI Pattern A (83 cases, 80%) was more frequent than pattern B (21 cases, 20%), for acute border zone infarctions, regardless of the cause.

### The proximal ICA stenosis or occlusion

Of the 45 cases, pattern A was observed in 34 cases (76%): 3 cases (9%) for the mild, 1 case (3%) for the moderate, 13 cases (38%) for the severe, and 17 cases (50%) for the near-complete or complete occlusion. Of the 45 cases, pattern B occurred in 11 cases (24%): 1 case (9%) was moderate, 2 cases (18%) were severe, and 8 cases (72%) were near-complete or complete occlusion. Pattern A (76%) was more frequent than pattern B

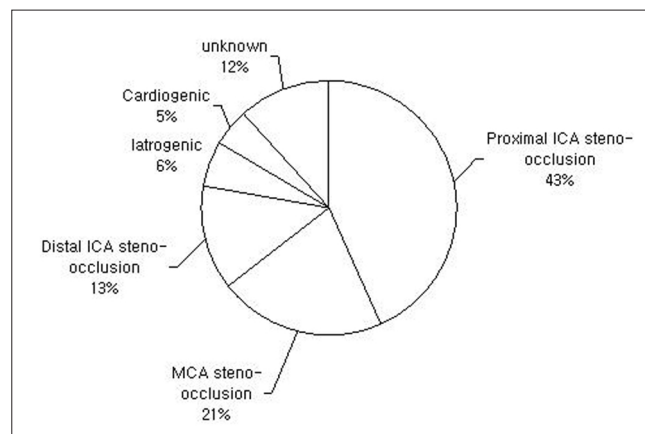
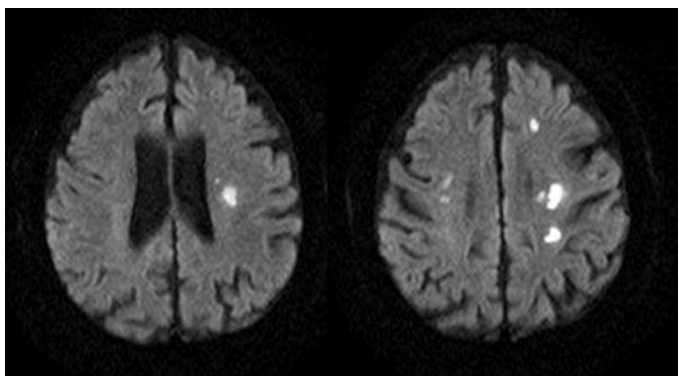


Fig. 3. The causes of an acute border zone infarction. ICA: internal carotid artery, MCA: middle cerebral artery.



A

Fig. 2. Pattern B: (A) Diffusion-weighted imaging shows bilateral acute internal border zone infarctions. No evidence of disseminated cortical infarctions are noted. (B) An MR angiography reveals severe stenosis of both the proximal and internal carotid arteries.



B

(24%), regardless of the degree of stenosis (Fig. 4).

#### **The MCA stenosis or occlusion**

A total of 14 patients underwent a MCA stenosis: 12 patients (86%) showed pattern A and 2 patients (14%) showed pattern B. A total of 8 patients underwent a MCA occlusion: 5 patients (63%) showed pattern A and 3 patients (37%) showed pattern B. Of the 22 patients with MCA stenosis or occlusion, DWI revealed pattern A in 17 cases (77%) and pattern B in 5 cases (23%) (Fig. 5).

#### **The distal ICA stenosis**

Eleven (79%) out of 14 patients with ICA stenosis showed the pattern A, whereas 3 patients (21%) showed the pattern B.

#### **Iatrogenic origin**

Six patients with a history of a conventional angiography demonstrated an acute border zone infarction, in all patients displaying pattern A. A conventional angiography was performed to evaluate the vascular lesions, including intra-or extra-cranial artery stenoses, aneurysms or arteriovenous malformations. The tested patients had no prior history of neurologic symptoms or acute infarction on DWI before performing a conventional angiography. The patients complained of minor neurologic symptoms after a conventional angiography. Moreover, the DWI showed abnormally high intensity signals in the border zone and the cerebral cortex; however, all patients recovered free of any neurologic deficits.

#### **Cardiogenic cause**

All five patients exhibited pattern A. Of these, three patients had atrial fibrillation, whereas two patients had left atrial thrombi on an ECG and echocardiography.

#### **Unknown cause**

A total of 12 patients (pattern A: 10 patients, pattern B: 2 patients) had an acute border zone infarction due to unknown causes. No evidence of vascular abnormalities on MRA or cardiac abnormalities on ECG and echocardiography were observed. As well, hematologic studies performed on patients showed no abnormalities.

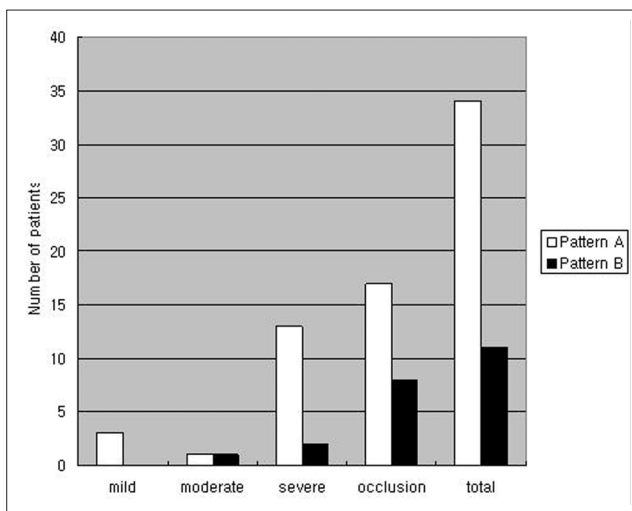
#### **TCD study**

A TCD study was performed in 75 of the 104 patients. Of the 75 patients, 7 (11%) showed at least 1 embolic pulse. All cases showed severe stenosis of the proximal ICA.

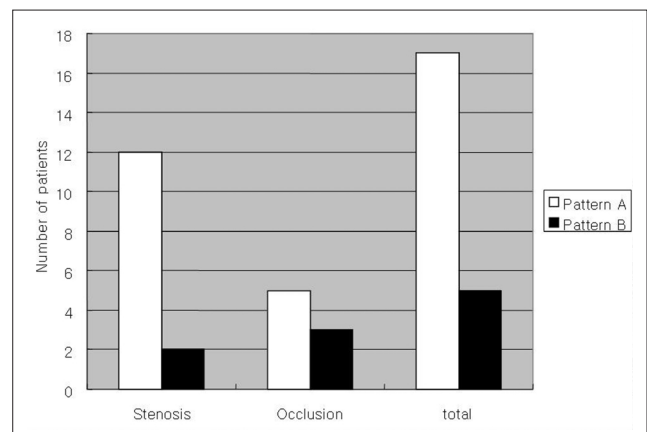
### **Discussion**

Border zone infarctions are classified as either internal or external border zone infarctions. The internal border zone is located between the medullary penetrators, from the pial-middle cerebral artery system, and the deep perforating lenticulostriate branches of the MCA. The external border zone is located in the pial arteriole, between ACA and MCA, as well as the PCA and MCA (9).

Efforts to identify the causes of border zone infarctions first began by performing autopsies. These studies revealed a cholesterol embolus in the border zone area.



**Fig. 4.** The graph reveals lesion patterns as a function of the degree of internal carotid artery stenosis. Pattern A is a dominant pattern regardless of stenosis degree.



**Fig. 5.** The graph reveals lesion patterns according to middle cerebral artery stenosis or occlusion. Pattern A is dominant pattern regardless of middle cerebral artery stenosis or occlusion.

The causes for the border zone infarctions were determined to be attributed to hypoperfusion and another cause (emboli) (7, 8, 10).

A CT showed that external border zone infarctions were rarely visible and evenly distributed among patients with embolisms from cardiac sources and severe carotid obstructions. Namely, the cortical wedge-type border zone infarctions, thought to result from hemodynamic factors compromise the low-flow perfusion locations, and may be seen in patients with cerebral embolisms and are furthermore hemodynamically compromised due to severe carotid disease. In contrast, internal border zone infarctions were significantly greater in patients with carotid obstructive disease than in cardiac embolisms (11). Moreover, embolisms have been suggested as the cause of border zone infarctions; however, the precise evidence of emboli on CT could not be identified.

The use of DWI, allowed us to outline the evidence for the emboli disseminated in the cerebral cortex. Based on this evidence, we classified the patterns comprising the acute border zone infarctions as well as analyzed them for the causes of the border zone infarctions. The degree of ICA stenosis significantly influenced the pattern of cerebral ischemia, as seen on a DWI. Multiple embolic lesions with high-grade ICA stenosis are a common feature of cerebral ischemia. The increasing degree of stenosis leads to additional hemodynamic alterations within the subcortical and cortical border zone areas (2). Moreover, severe ICA occlusive disease causes both an embolism and decreased perfusion. If blood flow currents are altered due to perfusion decreases, the microemboli will attain the recipients with blood vessels having the least effective blood flow. Decreased blood flow also likely impedes the clearance of emboli. Because perfusion is mostly impaired in the border zone regions, if an embolus reaches an arterial region, the clearance of emboli should be, for the most part, impaired in regions with the lowest blood flow (12). Furthermore, we think this to be the reason for the higher incidence of acute border zone infarctions with disseminated embolic signal intensities in the cortical region in patients with severe and nearly-complete or complete proximal ICA occlusion. Nevertheless, another investigator showed a different result, in patients with a 90% to 99% degree of ICA stenosis; the low post-stenotic flow fails to dislodge emboli from the plaque surface and carry them out distally, even if the plaque is unstable (13). At that point, another factor influencing acute border zone infarctions

should be considered: "Collateral circulation". In relatively undamaged primary collateral pathways, the cerebral blood flow does not decrease below the critical level required for acute border zone infarcts (13). Hence, we can postulate that the less a patient has to supply collateral circulation, the greater the chance for the occurrence of acute border zone infarctions. A perfusion-weighted image study, pertaining to border zone infarctions, revealed that artery to artery embolisms can cause small perfusion deficits in the border zone territory, which matches the area of diffusion abnormality. A large-artery occlusive disease is usually associated with large territorial perfusion deficits, unless collateral circulation exists and is predisposed to causing border zone infarctions (4). Hence, although the degree of ICA stenosis is the primary factor for border zone infarctions, we must evaluate the collateral circulation.

Similar to ICA stenosis or occlusion, multiple cerebral embolisms are also important mechanisms leading to cerebral infarcts in patients with MCA stenosis. The propensity for border zone infarcts indicates that hemodynamic compromise, in conjunction with multiple small emboli, may result in deep border zone infarctions, possibly due to the failure to clear emboli in a poorly perfused brain area (14). In atherosclerotic MCA territory infarctions, concomitant small cortical or subcortical lesions are also commonly associated findings of the diverse patterns comprising MCA territory infarctions, which can be explained by probable embolic mechanisms (3).

Intensive care must be provided to a patient with an acute border zone infarction, because upwards of 40% of patients with acute border zone infarctions had a degenerative clinical course (15).

Cardiac infarctions can cause large hemispheric infarctions and border zone infarctions. In patients with the acute border zone infarctions, all patients had a disseminated cortical infarction. This means that if small fragmented emboli are disseminated, border zone and cortical infarctions are induced. In a TCD study involving acute border zone infarction patients, cortical and subcortical high signal intensities were more frequently seen in patients with multiple embolic signals and large-vessel occlusive disease than in patients without microemboli (16, 17). In our study, 7 out of 75 patients had at least 1 embolic signal during the TCD study. This finding also supports the hypothesis that emboli are one of the common causes of border zone infarctions.

In particular, we have observed acute border zone in-

farctions with disseminated cortical infarctions in patients subjected to a conventional angiography. These patients had no apparent vascular stenosis or occlusion with an angiography and additionally, did not have any sources of cardiogenic embolisms. Despite the few amount of cases, we can nonetheless postulate that emboli alone could cause border zone infarctions.

The limitations of this study include: 1) not fully evaluating the collateral flows, 2) since the exact border zone is not always the same from person to person, we must consider the variation in location between the vascular territories of the major cerebral arteries.

In conclusion, the cause of border zone infarctions is variable and, no matter what the cause of acute border zone infarctions, pattern A was more common than pattern B. We propose that the mechanisms driving acute border zone infarctions are embolism coupled with hypoperfusion. This determination will aid in treatment of patients with acute border zone infarctions.

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